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Stockholm, March 14, 1960

Professor Joshua Lederberg
Department of Genetics
Stanford University
Palo Alto, California
USA

Dear Joshua:

In an earlier letter, dated December 1, 1959, you have kindly asked me whether there was any likelihood of my visiting the United States during this year. You mentioned your series of Transplantation Seminars as a possible excuse. At that time I had no plan of going to the States this year, but in a weak moment I have now accepted an invitation to participate at a symposium in Bar Harbor September 9 and 10 this year. The symposium will deal with methodology in mammalian genetics. If you have any plans to come there, I should be most happy if I could see you and we could discuss the arrangements for 1961. Alternatively, if you have any possibility of coming over here during your trip to London, I am sure that we could manage to obtain funds for financing your and Esther's trip from London to Stockholm and back. If neither of these possibilities works out, however, I should be happy if the transplantation seminar mentioned in your letter could be arranged so that I could visit you in September. As usual, my time will be probably very limited but I suppose that the jet communications permit quite rapid movement nowadays. My trip to and from Bar Harbor will be financed by the symposium but I would need financial covering of the transcontinental trip. Since I shall ask the Cancer Society here for our 1961 trip for a travel grant, I would hesitate to ask them for this supplementation now.

We have some interesting results regarding the development of H-2 reactivity in different cells in newborn animals. As you know, humoral H-2-isoantibodies will rapidly kill lymph node cells, bone marrow cells, ~~erythrocytes,~~ lymphoma cells and lyse erythrocytes, all in the presence of complement, while epithelial and connective tissue cells, carcinomas and sarcomas do not react very much or at all. In newborn mice of several strains erythrocytes cannot be agglutinated with H-2 isoantibodies and agglutinability develops only after 3-6 days. This was generally assumed to be due to the lack of H-2 isoantigens on these cells. A student of mine, Göran Möller has made some experiments and it turns out that spleen cells are not sensitive either to the cytotoxic action of humoral isoantibodies in these strains during the first three days of life but become sensitive at about

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the same time or somewhat earlier as agglutinability of the red cells develops. The same behavior is shown by bone marrow cells. The lack of cytotoxic sensitivity of the spleen and bone marrow cells is not due to the lack of H-2 isoantigens, however, since they will absorb H-2 isoantibodies specifically and rapidly and to the same extent as do adult cells. There is a difference in their reactivity rather than in their antigenicity.

We were speculating whether there might be any correlation between the sensitivity of the spleen and bone marrow cells to cytotoxic antibodies and the time at which the animals start to develop their immune reactivity. For this reason we have studied the cytotoxic sensitivity in spleen cells of newborn mice of strains where tolerance cannot be induced when newborn, namely C57Bl and C57 leaden. It turned out that spleen cells have already fully developed cytotoxic sensitivity in these mice when newborn. In those strains where the newborn cells do not show any sensitivity, (C3H, A, CBA, etc.), sensitivity develops concurrently with the change of the animal from the tolerance-inducible to the immune-reactive state (3-6 days). Also, a quick survey of the litterature indicates that the appearance of hemagglutinability of red cells by isoantibodies appears at different times in different species and there seems to be a rough correlation with the period during which the inducibility of tolerance disappears.

These are the facts. We have been speculating whether this could be interpreted so that at the time when the ability of the immunologically competent cells to form antibodies develops, they change in some fundamental respect related to the uptake of proteins, including antigens and antibodies, from their medium. All cells have H-2 isoantigens on their surface and can absorb H-2 isoantibodies from a medium; but only those would really take up antibody and become damaged by it which have reached a state of differentiation that made them competent for antibody formation. Does this sound completely crazy to you? We shall be delighted to send you the facts; Möller is just writing them up.

With warmest regards,

Yours as ever,

George Klein

GK/APT